

Application No.: 10/705,665

Docket No.: 21581-00240-US1

**REMARKS**

Claims 1-3 and 5-18 are now in the application. Claims 1, 6 and 10 have been amended to recite "adding" in place of "permitting;" by deleting "act upon" and inserting "to conduct reaction" for purposes of clarification and not to limit the scope of claim 1.

Support for the amendments in claims 1 and 6 can be found in the specification at column 8 lines 20-23 that state "the reaction can be conducted by ~~~ adding the lithium amide solution dropwise to the reaction mixtures".

Claim 17 has been amended to recite "the 3-hydroxypropionic acid derivative of the formula (II) or the 5-hydroxy-3-oxopentanoic acid derivative of the formula (IV) in place of "compound (II) or (VI) for purposes of clarification and not to limit the scope of claim 17. This amendment is to render claim 17 consistent with claim 1 from which it depends.

Claim 18 has been amended to recite "the acetic acid ester of the formula (I) in place of "the acetic acid ester" for purposes of clarification and not to limit its' scope. This amendment is based on recitations in claim 1.

The Abstract has been replaced by the Abstract included in this response.

The prior amendment to claim 1 was proper no matter was deleted therefrom. Instead, claim 1 was amended by reciting, "in the presence of a magnesium halide" which was underlined as required.

The rejections of the claims 1-3, 5 and 17-18 under 35 USC 112 have been overcome by the amendments to the claims and/or are not deemed tenable. In particular, claims 1, 6 and 10 have been amended to recite positive process steps, namely, the process of now-amended claims 1, 6 and 10 comprises adding a lithium amide to a mixture to conduct reaction. Thus, claims 1, 6 and 10 and those claims dependent there from are definite.

The rejections of claims 1-3, 5 and 14-18 as "no R<sup>3</sup> in the structure set forth" are not deemed tenable. R<sup>3</sup> in the formula (II) is defined in claim 1, fifth line to second line from the bottom of the claim ("R<sup>3</sup> represents any of an alkyl group of 1 to 12 carbon atoms, an aryl group

Application No.: 10/705,665

Docket No.: 21581-00240-US1

of 6 to 12 carbon atoms and an aralkyl group of 7 to 12 carbon atoms; and  $R^2$  and  $R^3$  may be joined to each other to form a ring").

The recitation "the compound (II) or (IV)" recited in claim 17 has been amended based on the recitation of claim 1.

The limitation "acetic acid ester" recited in claim 17 has been amended based on the recitation of claim 1.

The limitation "acetic acid ester" recited in claim 18 has been amended based on the recitation of claim 1.

Claims 10-13 were rejected under 35 USC 103(a) as being unpatentable over US patent 4,970,313 to Wess et al. Wess et al fail to render obvious claims 10-13.

Wess suggests (Example 2, column 9, lines 1-25) a process comprising:

- 1) adding t-butyl acetate to mixture of lithium diisopropylamide (formed in situ), which is cooled to  $-70^{\circ}\text{C}$ , to prepare a lithium enolate,
- 2) adding S-3-hydroxy-4-(t-butyldiphenylsilyloxy) butyrate (the compound of Example 1) at  $-70^{\circ}\text{C}$ , to conduct coupling reaction, and
- 3) then allowing the temperature of the mixture to rise slowly to  $-15^{\circ}\text{C}$ .

On the other hand, the process of claim 10 of the present application comprises:

- 1) Preparing, in advance, a mixture of an acetic acid ester of the formula (I) and magnesium alcoholate of the formula (VI), and
- 2) Then adding lithium amide of the formula (III) at a temperature not below  $-20^{\circ}\text{C}$  to the mixture to conduct reaction.

Application No.: 10/705,665

Docket No.: 21581-00240-US1

Thus, Wess only suggests that addition of materials may be carried out at  $-70^{\circ}\text{C}$ . The addition at a temperature not below  $-20^{\circ}\text{C}$  is not obvious from Wess et al and is contrary to the suggestions therein.

The reason why the process of Wess essentially requires a low temperature condition involves the formation of a lithium enolate in the first step. Lithium enolates are quite unstable except for at very low-temperatures. Therefore, to avoid decomposition thereof, the substrate ester has to be added to the lithium enolate at an extremely low temperature.

On the other hand, the process of claim 10 comprises adding a lithium amide to the mixture of an acetic acid ester (I) and magnesium alcoholate of the formula (VI). According to the process, an enolate is consumed as soon as it is formed in situ, by the reaction with magnesium alcoholate of the formula (VI). Thus, control of stability of the enolate is not required, and such a low temperature condition as  $-70^{\circ}\text{C}$  is not necessary for conducting a reaction.

Furthermore, use of magnesium alcoholate of the formula (VI) also stabilizes the product 5-hydroxy-3-oxopentanoic acid derivative of the formula (IV) in the reaction mixture. As a result, the process of the present invention realizes a high yield even if at such a relatively higher temperature as  $-20^{\circ}\text{C}$  or higher. It is found that the product usually tends to be decomposed at around  $20^{\circ}\text{C}$  in the reaction. If magnesium alcoholate were not used in this process, the yield would be drastically decreased because of decomposition during the reaction. Use of the magnesium alcoholate, however, stabilizes the product, leading to high product yield. Such an effect of the present invention cannot be expected from Wess.

Thus, addition at a temperature not below  $-20^{\circ}\text{C}$  is not obvious from Wess at all. Furthermore, it cannot be expected from Wess at all that the process of the present invention makes it possible to realize a high-yield production of a 5-hydroxy-3-oxopentanoic acid derivative of the formula (IV) even at a relatively higher temperature as  $-20^{\circ}\text{C}$  or higher.

Consequently, the invention of claims 10-13 is not obvious over Wess et al.

Application No.: 10/705,665

Docket No.: 21581-00240-US1

Claims 6-9 were rejected under 35 USC 103(a) as being unpatentable over US patent 4,970,313 to Wess et al. in view of Solomon's Organic Chemistry, fifth edition, 1992, John Wiley & Sons, pgs. 461-462. The cited references fail to render obvious Claims 6-9. The above discussion of Wess et al. is incorporated wherein by reference. The reasons discussed above concerning the patentability of claim 10-13 are also applicable to claims 6-9.

Namely, the invention recited in claim 6 comprises adding lithium amide at a temperature not below -20°C, which is not obvious from Wess et al. and the process makes it possible to realize a high-yield production of a 5-hydroxy-3-oxopentanoic acid derivative of the formula (IV) even at a relatively higher temperature as -20°C or higher, which not expected from Wess et al.

Solomon failed to overcome the above discussed deficiencies of Wess et al. with respect to rendering obvious claims 6-9. Solomon was relied upon for a disclosure that an alcohol reacts with a Grignard reagent to yield the corresponding halo magnesium alcoholate and the corresponding hydrocarbon.

The mere fact that cited art may be modified in the manner suggested by the Examiner does not make this modification obvious, unless the cited art suggest the desirability of the modification. No such suggestion appears in the cited art in this matter. The Examiner's attention is kindly directed to *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 2002) *In re Dembiczak et al.* 50 USPQ2d. 1614 (Fed. Cir. 1999), *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984), *In Laskowski*, 10 USPQ2d. 1397 (Fed. Cir. 1989) and *In re Fritch*, 23, USPQ2d.1780 (Fed. Cir. 1992).

In *Dembiczak et al.*, supra, the Court at 1617 Stated: "Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., *C.R. Bard, Inc., v. M3 Sys., Inc.*, 157 F.3d. 1340, 1352, 48 USPQ2d. 1225, 1232 (Fed. Cir. 1998) ('the Board must identify specifically... the reasons one of ordinary skill in the art would have been motivated to select the references and combine them');...".

Application No.: 10/705,665

Docket No.: 21581-00240-US1

Also, the cited art lacks the necessary direction or incentive to those of ordinary skill in the art to render the rejection under 35 USC 103 sustainable. The cited art fails to provide the degree of predictability of success of achieving the properties attainable by the present invention need to sustain a rejection under 35 USC 103. See *Diversitech Corp. v. Century Steps, Inc.* 7 USPQ2d 1315 (Fed. Cir. 1988), in *re Mercier*, 185 USPQ 774 (CCPA 1975) and *In re Naylor*, 152 USPQ 106 (CCPA 1966).

Moreover, the properties of the subject matter and improvements which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 USC 103. See *Gillett Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d. 1923 (Fed. Cir. 1990), *In re Antonie*, 195, USPQ 6 (CCPA 1977), *In re Estes*, 164 USPQ 519 (CCPA 1970), and *In re Papesch*, 137 USPQ 43 (CCPA 1963).

No property can be ignored in determining patentability and comparing the claimed invention to the cited art. Along these lines, see *In re Papesch*, supra, *In re Burt et al.*, 148 USPQ 548 (CCPA 1966), *In re Ward*, 141 USPQ 227 (CCPA 1964), and *In re Cescon*, 177 USPQ 264 (CCPA 1973).

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

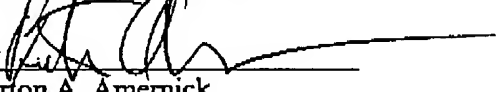
Application No.: 10/705,665

Docket No.: 21581-00240-US1

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 22-0185, under Order No. 22116-00002-US2 from which the undersigned is authorized to draw.

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Respectfully submitted,

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